REMARKS

Summary of Interview Pursuant to 37 C.F.R. § 1.133(b)

The Applicant wishes to thank the Examiner for the telephone interview on June 3, 2010. The outstanding obviousness rejection was discussed with respect to clarification on how the reasoning regarding secretions applied to Claim 34. The Examiner and Applicant agreed to a subsequent telephone interview around the middle of July once the present response was filed and assigned to the Examiner's docket.

Amendments to the Claims

Claims 11 and 34-44 are pending. The Applicant respectfully asks the Examiner to replace all prior versions and listings of claims in the present application with the listing of claims currently provided. Claims 11, 34-40, 42, 43, and 44 were amended. The Applicant states that all amended claims do not add new subject matter to the present specification.

Claim 11 amendment support can be found at, *e.g.* ¶¶ 104, 110.

Claim 34 amendment support can be found at, *e.g.* ¶¶ 124, 125.

Rejection Pursuant to 35 U.S.C. § 103(a) Obviousness

The Examiner has rejected Claims 11 and 34-44 as allegedly being obvious under 35 U.S.C. § 103(a) over Aoki, et al, *Method for Treating Cervical Dystonia with Botulinum Type B*, U.S Patent Publication 2001/0043930, hereafter the "Aoki publication," in view of Wald and Kakulus, *Apocrine Gland Carcinoma (Sweat Gland Carcinoma) of the Breast*, Australian New Zealand J. Surg. 33(3): 200-204 (1964), hereafter the "Wald reference" and Donovan, *Botulinum Toxin Implant*, U.S. Patent 6,312,708, hereafter the "Donovan patent" as evidenced by Vakil, *Etiology of Breast Cancer: I. Genetic Aspects*, C.M.A. J. 109: 29-32 (1973), hereafter the "Vakil reference."

The present Claim Set has three independent claims directed towards treating a mammary gland disorder by administration of a botulinum toxin type A.

Claim 11 is directed, in part, to a method for treating a mammary gland disorder associated with hyperplastic or hypertonic mammary gland tissue, wherein administration of the botulinum toxin type A causes the regression or remission of the hyperplastic or hypertonic tissue, or reduces the ability of the hyperplastic or hypertonic tissue to develop into a neoplasm, thereby treating the mammary gland disorder.

Claim 34 is directed, in part, to a method for treating a breast cyst, sclerosing adenosis, duct papilloma, fibroadenoma, blunt duct adenosis, and proliferative breast disease, wherein administration of the botulinum toxin type A causes a reduction in size of the breast cyst, sclerosing adenosis, duct papilloma, fibroadenoma, blunt duct adenosis, or proliferative breast tissue, thereby treating the mammary gland disorder.

Claim 45 is directed, in part, to a method for treating a mammary gland disorder associated with precancerous mammary gland tissue, wherein administration of the botulinum toxin type A causes a reduction in the size or activity of the precancerous mammary gland tissue, thereby treating the mammary gland disorder.

The Aoki publication is cited as disclosing the administration of a botulinum toxin type A to a patient suffering from abnormal secretions like excessive sweating, lacrimation (eye tearing), and mucus secretions. Aoki at ¶ 14; Example 5.

Although the Wald reference is cited as disclosing that apocrine gland carcinomas of the breast release a substance (see, e.g., May 4, 2007 Office Action p. 3, ¶ 2, lines 1-2; January 6, 2010 Office Action at p. 4, ¶ 1, lines 4-6), a close reading of this reference indicates that this is not correct. The cited disclosure of the Wald reference at p. 203, col. 1, last paragraph refers to a previous study reporting that normal apocrine glands of the breast secrete a substance. There is no evidence in the Wald reference that that a carcinoma of a breast apocrine gland continues to secrete a substance once it dedifferentiates into malignant cells. In fact, based on commonly accepted views in the art on carcinogenesis, cancerous cells

occur either by 1) stem cells that lose control of there cell growth regulatory mechanisms (stem cells are undifferentiated cells that give rise to multiple cell types upon differentiation); or 2) differentiated cells that that lose control of there cell growth regulatory mechanisms and become proliferative by regressing into a more undifferentiated state. In either case, these cancerous cells are rapidly dividing undifferentiated cells, and to that end, would not exhibit typical characteristics of differentiate cells, such as producing substances that would be secreted by a mature gland cell. As such, the Wald reference simply discloses that normal apocrine glands of the breast secrete a substance and is completely silent on whether a carcinoma cells derived from breast apocrine gland cells also secrete a substance.

The Vakil reference is cited as disclosing that secretions are emitted from normal apocrine gland cells from mammary glands.

The Donovan patent is cited as disclosing a biodegradable polymer implant capable of releasing botulinum toxin type A.

A. The cited references would not motivate combination of cited references.

The cited references, either alone or in combination, would not lead an artesian of ordinary skill to the presently claimed methods, and as such, the present methods are not obvious over the cited references.

For example, Aoki merely discloses that administration of a botulinum type A can inhibit excessive sweating, tearing or mucus secretions. The Wald and Vakil references merely discuss that normal apocrine gland cells of the mammary glands secrete a substance. The Donovan patent discusses that botulinum toxin type A can be administered via an implant. However, the cited references do not teach, suggest, or motivate one of ordinary skill to treat a precancerous mammary gland disorder by administering a botulinum toxin type A in order to 1) cause regression or remission of the hyperplastic or hypertonic tissue, or reduce the ability of the hyperplastic or hypertonic tissue to develop into a neoplasm; 2) cause a reduction in the size of the breast cyst, sclerosing adenosis, duct papilloma, fibroadenoma, blunt duct adenosis, or proliferative breast tissue; and/or 3) cause a reduction in the size or activity of the

precancerous mammary gland tissue.

As such, a person of ordinary skill would not be lead to the presently claimed methods because there is no nexus between the presently claimed methods and the cited references.

B. No reasonable expectation of success

Furthermore, the cited references, alone or in combination, provide no reasonable expectation of success that administration of a botulinum toxin type A. "The mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art." *MPEP* § 2143.01 (citing *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1396 (2007)).

In this case, one of ordinary skill in the art would not reasonable expect that administration of a botulinum toxin type A as a breast precancer therapy based merely on the findings that this toxin can inhibit excessive sweating, tearing or mucus secretions and normal apocrine gland cells of the breast secrete a substance. "Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness." MPEP § 2143.02(II)(citing *In re Rinehart*, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976)).

As such, there is nothing of record indicating that a person of ordinary skill would have a reasonable expectation that the presently claimed methods of treating precancerous mammary gland disorders would succeed based on the cited references as these references simply disclose how to treat gland disorders involving secretions that have no relationship to mammary gland disorders that develop into cancer.

C. Conclusion

The Applicant respectfully submits that currently amended claims are not obvious over the cited art. Therefore, the Applicant respectfully requests withdrawal of the 35 U.S.C. § 103(a) obviousness rejection against Claims 11 and 34-44.

CONCLUSION

For the above reasons the Applicant respectfully submits that the claims are in condition for allowance, and the Applicant respectfully urges the Examiner to issue a Notice to that effect. The Examiner is invited to call the undersigned attorney if there are questions.

Please use Deposit Account 50-3207 for the payment of any extension of time fees under 37 C.F.R. § 1.136 or any other fees due in connection with the current response.

Respectfully submitted,

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